Biological Psychology 104 (2015) 163–172

Contents lists available at ScienceDirect

Biological Psychology

journal homepage: www.elsevier.com/locate/biopsycho

# The effect of experimental sleep fragmentation on error monitoring

Cheng-Hung Ko[a], Ya-Wen Fang[a], Ling-Ling Tsai[a,*], Shulan Hsieh[b,c,**]

[a] Department of Psychology, National Chung Cheng University, Chiayi, Taiwan, ROC
[b] Department of Psychology, National Cheng Kung University, Tainan, Taiwan, ROC
[c] Institute of Allied Health Sciences, National Cheng Kung University, Tainan, Taiwan, ROC

ARTICLE INFO

*Article history:*
Received 2 April 2014
Accepted 15 December 2014
Available online 23 December 2014

*Keywords:*
Sleep disruption
Microarousal
Attention
Action monitoring
Cognitive performance

ABSTRACT

Experimental sleep fragmentation (SF) is characterized by frequent brief arousals without reduced total sleep time and causes daytime sleepiness and impaired neurocognitive processes. This study explored the impact of SF on error monitoring. Thirteen adults underwent auditory stimuli-induced high-level (H) and low-level (L) SF nights. Flanker task performance and electroencephalogram data were collected in the morning following SF nights.

Compared to LSF, HSF induced more arousals and stage N1 sleep, decreased slow wave sleep and rapid-eye-movement sleep (REMS), decreased subjective sleep quality, increased daytime sleepiness, and decreased amplitudes of P300 and error-related positivity (Pe). SF effects on N1 sleep were negatively correlated with SF effects on the Pe amplitude. Furthermore, as REMS was reduced by SF, post-error accuracy compensations were greatly reduced.

In conclusion, attentional processes and error monitoring were impaired following one night of frequent sleep disruptions, even when total sleep time was not reduced.



## 1. Introduction

Performance monitoring is critical for maintaining satisfactory operations when completing a task. Error monitoring is a core cognitive process of performance monitoring and is responsible for real-time surveillance of performance accuracy. If a response error does occur, an optimally functioning error monitoring system will detect the error, enforce an immediate corrective behavior (Fiehler, Ullsperger, & von Cramon, 2004) to limit the impact of the response error, and/or employ behavioral adjustments to response strategy, e.g., slowing down response speed (Rabbitt, 1966), to prevent response errors from recurring in the near future (Laming, 1968, 1979).

Sleep loss during extended wakefulness over a night results in attenuation in the amplitude of two erroneous event-related brain potential (ERP) components, the error-related negativity (ERN) (Hsieh, Cheng, & Tsai, 2007; Hsieh, Li, & Tsai, 2010; Ramdani et al., 2013; Renn & Cote, 2013; Scheffers, Humphrey, Stanny, Kramer, & Coles, 1999; Tsai, Young, Hsieh, & Lee, 2005) and the subsequent error positivity (Pe) (Asaoka, Fukuda, Murphy, Abe, & Inoue, 2012; Hsieh et al., 2007, 2010; Murphy, Richard, Masaki, & Segalowitz, 2006; Tsai et al., 2005), and impairs several behavioral outcomes of error monitoring, e.g., error correction (Hsieh et al., 2007; Hsieh, Tsai, & Tsai, 2009), post-error slowing (Murphy et al., 2006), and post-error improvement in response accuracy (Hsieh et al., 2010; Tsai et al., 2005). The ERN amplitude decreases as the number of response errors increases and is thought to reflect processes of error detection and post-error compensation (Gehring, Goss, Coles, Meyer, & Donchin, 1993). The Pe represents a later aspect of error processing distinct from the early ERN component and is associated with error awareness (Murphy, Robertson, Allen, Hester, & O'Connell, 2012; Nieuwenhuis, Ridderinkhof, Blom, Band, & Kok, 2001), emotional evaluation of errors (Hajcak, McDonald, & Simons, 2003), and post-error slowing (Hajcak et al., 2003; Nieuwenhuis et al., 2001). The Pe appears more sensitive to sleepiness resulting from mild sleep loss or sleep disruption than the ERN since the Pe amplitude is reduced but the ERN amplitude remains unchanged after 20 h of extended wakefulness, approximately 3 h nighttime sleep loss (Asaoka et al., 2012; Murphy et al., 2006). Furthermore, monetary incentives successfully counteract the effect of total sleep deprivation for a night on the ERN amplitude but fail to rescue reduced Pe amplitude (Hsieh et al., 2010).

* Corresponding author at: Department of Psychology, National Chung Cheng University, 168 University Road, Minhsiung Township, Chiayi County 62102, Taiwan, ROC. Tel.: +886 5 2720411x32201; fax: +886 5 2720857.
** Corresponding author at: Control, Aging, Sleep, Emotion (CASE) Laboratory, Department of Psychology, College of Social Sciences, Institute of Allied Health Sciences, College of Medicine, National Cheng Kung University, 1 University Road, Tainan 701, Taiwan, ROC. Tel.: +886 6 2008703.
*E-mail addresses:* psyllt@ccu.edu.tw (L.-L. Tsai), psyhsl@mail.ncku.edu.tw (S. Hsieh).

http://dx.doi.org/10.1016/j.biopsycho.2014.12.008
0301-0511/

In contrast to total sleep deprivation, experimental sleep fragmentation (SF) represents frequent disruptions of sleep with total sleep time remaining unchanged or slightly reduced. Experimental SF is set to be a model for the type of frequent and periodic sleep disruptions experienced with common sleep problems where the sleeper may be aroused several hundred times in sleep by intrinsic stimuli such as sleep-related breathing and movement problems, extrinsic stimuli such as continuous environmental noises, or a combination of both intrinsic and extrinsic stimuli. The degree of SF varies with the frequency of sleep-disturbing stimuli and the arousal response induced by the stimuli. Several studies of experimental SF produced by using tones or other sensory stimuli to induce brief arousals or awakenings found changes in physiological and behavioral function similar to those found after total sleep deprivation (reviewed in Bonnet & Arand, 2003; Reynolds & Banks, 2010; Stepanski, 2002). Even if the total sleep time is maintained, one or two nights of SF still result in increases in sympathetic nervous system and adrenocortical activity (Stamatakis & Punjabi, 2010), negative mood valence (Kingshott, Cosway, Deary, & Douglas, 2000; Martin, Engleman, Deary, & Douglas, 1996; Martin, Wraith, Deary, & Douglas, 1997), daytime sleepiness (Kingshott et al., 2000; Martin et al., 1996, 1997; Philip, Stoohs, & Guilleminault, 1994; Roehrs, Merlotti, Petrucelli, Stepanki, & Roth, 1994; Stepanski, Lamphere, Roehrs, Zorick, & Roth, 1987), decreases in glucose metabolism (Stamatakis & Punjabi, 2010), positive mood valence (Martin et al., 1996, 1997), and psychomotor and cognitive performance (Martin et al., 1996; Stepanski et al., 1987). However, the effect of SF on cognitive performance was not consistently supported by other studies using similar protocols of tone-induced SF (Cote, Milner, Osip, Ray, & Baxter, 2003; Kingshott et al., 2000; Philip et al., 1994; Roehrs et al., 1994) even when using the same cognitive tasks (Kingshott et al., 2000; Martin et al., 1996). The ERP appears to be a more sensitive measure of cognitive processing than the behavioral response in terms of the ability to detect the cognitive deficit resulting from sleep disturbances. For example, the amplitude of the P300, which is related to attentional processes (reviewed in Picton, 1992; Polich, 2007), is reduced following a night of experimental SF, despite the unchanged behavioral response (Kingshott et al., 2000). The P300 and Pe are intimately related to each other (Davies, Segalowitz, Dywan, & Pailing, 2001) and reflect similar neurocognitive processes referring to the motivational significance of salient events (Ridderinkhof, Ramautar, & Wijnen, 2009). As mentioned above, monetary incentives effectively maintain the ERN amplitude after sleep deprivation but fail to rescue reduced Pe as well as P300 amplitudes (Hsieh et al., 2010).

This study aimed to explore the error monitoring system's vulnerability to sleep disturbances other than total sleep deprivation. We applied the auditory stimuli-induced SF protocol and carefully minimized the reduction in total sleep time with normal night sleep (Martin et al., 1996). Contrary to previous experimental SF procedures that included an SF night and a control undisturbed night, we designed two protocols for auditory stimuli presentation to induce a low-level and a high-level SF (LSF and HSF) respectively. The LSF night served as a control condition for frequent but mild sleep-disturbing auditory stimulation during sleep. We then examined whether the ability of error monitoring while performing a flanker task (Eriksen & Eriksen, 1974) differed between the two SF conditions. To compare the SF effect in this study with previous SF studies, we included two cognitive tasks, the Continuous Performance Test (CPT) (Rosvold, Mirsky, Sarason, Bransome, & Beck, 1956) and the Paced Auditory Serial Addition Task (PASAT) (Gronwall, 1977), and the P300 measures which were all previously found to be affected or related to SF (Kingshott et al., 2000; Martin et al., 1996; Sadeh, Gruber, & Raviv, 2002). Last, given that SF manipulations might cause nonspecific stress responses, in addition to sleep disruption, we took several stress measures, such as subjective evaluation, salivary cortisol concentration, and heart rate, to evaluate stress responses to SF manipulations.

We expected that one night of HSF would increase daytime sleepiness and reduce cognitive controls in attention and error monitoring.

## 2. Material and method

### 2.1. Participants

Normal volunteers were recruited from local universities and communities through recruitment advertisements for the study. A total of 185 volunteers responded and underwent questionnaire interviews. Of them, 39 volunteers were between the ages of 20 and 35 years, right-handed, and nonsmokers; they had a body-mass index (BMI) within 17 and 25 $kg/m^2$, a senior high school degree or higher, and normal or corrected-to-normal vision. Furthermore, they did not have any history of medical, psychiatric, sleep-related disorders, and traumatic head injury nor were they currently using any medications or drugs. They were not regular liquor drinkers. They did not work at night or on a rotating shift schedule, or travel in the previous month or plan to travel in a recent month across multiple time zones. They self-reported regular sleep patterns with mean sleep latency <30 min, daily sleep duration ≥7 h, and daily bedtime varying ≤2 h. They were free from any complaint of SF. They had Epworth Sleepiness Scale (ESS) scores (Johns, 1991) ≤11, Owl and Lark Questionnaire (OLQ) scores (Horne & Ostberg, 1976) within 42–58 (intermediate type), Beck Anxiety Inventory (BAI) scores (Beck, Epstein, Brown, & Steer, 1988) ≤7 and Beck Depression Inventory-II (BDI-II) scores (Beck, Steer, & Brown, 1996) ≤13. Only 28 of the 39 volunteers agreed to receive the laboratory overnight polysomnography, and 18 of them fulfilled all the inclusion criteria, including sleep efficiency ≥90%, periodic limb movement index ≤15 per hour slept, arousal index ≤10 per hour slept, apnea and hypopnea index ≤5 per hour slept, bruxism index ≤1 per hour slept, and normal electrocardiogram (ECG). Only 14 of the 18 volunteers were willing to follow all the experimental procedures and provided informed written consent. All 14 participants were provided remuneration for their participation in the experiment. The study protocol was approved by the Institutional Human Subject Ethics Committee of National Chung Cheng University.

The data from 1 participant were excluded from statistical analyses. This participant was relatively unresponsive to auditory noises though her auditory response threshold in waking to 1000-Hz was 39 dB thus, slightly lower than the mean value (39.3 dB) obtained from the remaining 13 participants. Compared to a mean value of 165% and a minimum of 62% increased at the HSF night relative to the previous adaptation night, her arousal index was increased by only 23% even though the mean duration (121 s) and the mean volume (106 dB) used for the auditory stimuli were the highest values among all participants.

### 2.2. Procedure

Each participant underwent 2 experimental periods with a 1–3 week washout interval in a counterbalanced cross-over design. The 2 experimental periods for women participants were arranged close to the time between their mid-follicular and mid-luteal phases. Each experimental period started with a week of sleep log and actigraph (AW2 Actiwatch, Philips-Respironics-Mini Mitter, Bend, OR, USA) recordings at home during which the participants were instructed to maintain their regular sleep schedules and reminded by phone calls 1–2 times from a research assistant. The sampling rate of actigraph was set at 1 min per sample and analyzed using Actiware v.5 (Philips-Respironics-Mini Mitter). Participants then slept in a sleep laboratory for 2 pairs of 2 nights. The first night of each pair served as an adaptation night, during which participants were allowed to sleep uninterrupted. On the second night of each pair, sleep was disrupted by frequent auditory stimuli presented with a protocol to induce LSF or HSF. Lights-out times on the 4 nights for each participant were matched to their mean weekly bed time calculated from sleep logs and varied between 23:00 and 24:00. Lights-on times following the adaptation night and the LSF night for each participant were also matched to their mean weekly getup time and varied between 07:00 and 08:00. However, lights-on times following the HSF night were extended by 15 min to compensate for partial, if not all, possible lost sleep caused by the HSF manipulation.

Participants lying in bed evaluated their subjective stress levels (from 1 = extremely low to 10 = extremely high) right before lights-out on each night and, again, right after lights-on followed by sitting up in bed, giving saliva samples using Salivette Cortisol (Sarstedt), and evaluating sleep quality (from 1 = extremely poor to 10 = extremely good). After rising from bed each morning, participants took two cognitive tests, the CPT (Rosvold et al., 1956) and the PASAT (Gronwall, 1977); tests began approximately 30 min after lights-on and were followed by a caffeine-free breakfast.

Participants were prohibited from consuming caffeine and alcohol starting on the day before the adaptation night through the morning test period following the SF night. On the day following the adaptation night, they were free to leave and do routine daytime work but were instructed to take their habitual daytime naps 6 h before bedtime, have dinner 4 h before bedtime, to limit daily nap time to an hour or

less and high-intensity exercise time half an hour or less, and to refrain from high-intensity exercise after 17:00. Execution of these restrictions was assumed to limit the magnitude of fluctuations in daytime sleep debt accumulation and in circadian rhythms during the two laboratory study periods. On the day following the SF night and morning breakfast, each participant performed a modified flanker task (Eriksen & Eriksen, 1974) with arrow stimuli (Hsieh et al., 2009; Tsai et al., 2005) starting at approximately 10:00 (2.5 h after lights-on) in a sound-attenuated room with the lights switched off. Multiple-channel electroencephalogram (EEG) was recorded during the flanker task test. Participants evaluated their present sleepiness using the Stanford Sleepiness Scale (SSS) (Hoddes, Zarcone, Smythe, Phillips, & Dement, 1973) after they closed their eyes for 1 min at the time immediately before and, again, after the flanker task test. At the end of each flanker task test, they also answered 3 questions on subjective evaluations of task performance as described previously (Hsieh et al., 2009).

### 2.3. Polysomnography

For screening purposes, the laboratory overnight polysomnography was performed using the Easy II system (Cadwell Laboratories, Kennewick, WA) and included continuous recordings of the frontal (F4-M1/F3-M2), central (C4-M1/C3-M2), and occipital (O2-M1/O1-M2) EEG, right (E2-M1) and left (E1-M2) electrooculogram (EOG), chin and anterior tibialis electromyograms (EMG), modified Lead II ECG, oronasal airflow detected simultaneously by a thermal sensor and an air pressure transducer (Pro-Tech PTAF2, Philips Respironics, Murrysville, PA), thoracic and abdominal respiratory efforts detected by inductance plethysmography (Pro-Tech zRIP Sum RT, Philips Respironics), snores, body position, and oxygen saturation detected by pulse oximetry placed on the right index finger. Sleep stages, including non-rapid eye movement sleep (NREMS) stages N1 (with low amplitude, mixed-frequency EEG activity but free of 8–13 Hz alpha rhythm for more than 50% of an 30-s epoch), N2 (with sleep spindles or K-complexes unassociated with arousals), and N3 (containing 0.5–2 Hz, amplitude greater than 75 μV slow wave activity for no less than 20% of an epoch) and rapid eye movement sleep (REMS; with low amplitude, mixed-frequency EEG activity, low chin EMG tone, and REMs), EEG arousals (abrupt shift of EEG frequency that lasts at least 3 s, with at least 10 s of stable sleep preceding the change), apneas/hypopneas, leg movements, and bruxisms were scored according to the American Academy of Sleep Medicine standards (Iber, Ancoli-Israel, Chesson, & Quan, 2007). We used the respiratory rule VIII.4.A (≥30% drop in airflow signal amplitude and ≥4% oxygen desaturation from pre-event baseline) for defining hypopnea (Iber et al., 2007). On all 4 sleep study nights during the two experimental periods, only EEG, EOG, chin EMG, and ECG were recorded.

Each overnight polysomnographic recording was carried out by 2 trained sleep researchers. All polysomnographic data were independently and manually scored in 30-s epochs by 2 trained sleep researchers. When disagreement on certain scored epochs occurred, a consensus was reached through discussion between the 2 scorers and, if necessary, consulting a senior sleep researcher.

### 2.4. SF protocol

A digitally recorded 1000-Hz tone and a firecracker noise were used to fragment sleep. The SF protocol was performed as described previously (Martin et al., 1996) with some modifications. For LSF, a 10-s 1000-Hz tone was first given through a pair of speakers placed above and behind the head of the bed after 1 min of continuous non-N1 sleep from sleep onset and stopped earlier than set duration if an EEG arousal (lasting for at least 3 s) occurred within the 10 s or stopped when 10 s elapsed if there was no EEG arousal. The next tone was not given until 1 min of continuous non-N1 sleep occurred for the former condition or until 1 min of continuous sleep (including N1) elapsed for the latter condition. For HSF, the criterion for the time when the first tone after lights-off was given was the same as that of LSF, except that the first tone lasted for 12 s. However, a firecracker noise randomly interchanged with the tone for the next presentation. The duration and/or the volume of the tone/firecracker noise would be increased at a 2 s/2–5 dB step up to a maximum value of 5 min/119 dB for the next presentation if the previous stimulus did not induce any EEG arousal during the period of stimulus presentation and 10 s after the stimulus stopped. If an EEG arousal did occur during this period, the tone/noise stopped immediately and the duration and/or volume of the tone/noise were reset.

Response thresholds to the 1000-Hz tone in waking were determined for each participant on each HSF and LSF night before sleep. The volume of the 1000-Hz tone was maintained at the threshold level throughout the LSF night but varied to be at or above threshold on the HSF night.

### 2.5. Cognitive tasks

#### 2.5.1. CPT

The CPT measures sustained attention and involves higher executive control (Rosvold et al., 1956). The number of night-awakenings, reflecting the level of SF, is positively correlated with the number of CPT commission errors in school-age children (Sadeh et al., 2002). In this task, a single letter was presented every 1, 2, or 3 s in the center of a 21.5″ 16:9 LCD monitor (VX2239wm, ViewSonic, Taiwan) and lasted for 250 ms using an E-Prime-based program (E-Prime 2.0, Psychology Software Tools, Pittsburgh, PA). Participants sat approximately 90 cm from the monitor, and they were instructed to press the "space" key on the keyboard with their right index finger as fast as possible every time they saw a letter other than an X (non-target letter). After 18 practice trials, participants completed 3 blocks of 60 trials each. The 3 inter-trial intervals were randomized with equal probabilities in each trial block. Between the blocks, participants were allowed to take a 1-min break. Three CPT measures were obtained and included mean reaction time (RT) for correct responses to target letters, omission errors for target letters, and commission errors for the non-target letter X.

#### 2.5.2. PASAT

The PASAT measures sustained attention and information processing (Gronwall, 1977). A previous study found 1 night of SF with short arousals resulted in fewer correct additions on the PASAT 4-s test (Martin et al., 1996). A series of numbers varying from 1 to 29 were randomly broadcast at 4- and 2-s intervals through a speaker. Participants were required to sum the two most recent numbers and write their answers down on paper prior to the presentation of the next number for a response to be scored as correct. After both 4-s and 2-s practice blocks of 9 trials each, participants completed a 4-s block of 50 trials, took a 1-min break, and then finished a 2-s block.

### 2.6. Flanker task

The arrow version of Flanker task (Eriksen & Eriksen, 1974) has been used and described in our previous studies (Tsai et al., 2005; Hsieh et al., 2009). We further raised the brightness gradient between the centered target arrow and flanked arrows to enhance the interfering effect of the flankers. Briefly, each trial started with a fixation white cross '+' on a black background for 1 s. A horizontal visual array of 5 arrows appeared immediately after the fixation disappeared and lasted for 50 ms. The target arrow (size: 0.22 cm × 0.21 cm; R: 77, G: 77, B: 77) was in the center of the visual array and was flanked on each side by two arrows (medial flankers: 0.25 cm × 0.23 cm; R: 178, G: 178, B:178; lateral flankers: 0.30 cm × 0.25 cm; R: 255, G: 255, B:255) pointing in the same direction as the target (congruent) or in the opposite direction (incongruent). Congruent and incongruent trials were presented with equal probabilities. Participants were required to press a designated key on the keyboard in response to the target arrow with maximal speed and accuracy. The next trial started 2 s after a key press or 4 s after the presentation of the arrow stimuli of the preceding trial if there was no response. After 32 practice trials, participants completed 16 blocks of 64 trials each. Participants were allowed to take a 1-min break between the test blocks. Measures of mean RT, intra-individual RT variability defined as the standard deviation of RT in a test divided by the mean RT in that test, response accuracy, error rate, and omission rate were respectively calculated for each participant. Post-error compensatory effects were examined according to the traditional method by comparing the variable value in the trials following correct responses (post-correct trials) with that of the trials following erroneous responses (post-error trials). The magnitude of post-error compensation was defined as the difference in response values between post-error and post-correct trials. Recently, it has been argued that this traditional method to analyze post-error compensations on RT is vulnerable to confounds from global performance fluctuations over the course of an experiment, and a simple solution has been provided by using only those post-correct trials that are also pre-error trials and the associated post-error trials (Dutilh et al., 2012). Thus, we also used the method suggested by Dutilh et al. (2012) to examine the post-error compensatory effect on RT.

### 2.7. Multiple-channel EEG recording

During the flanker task performance, in addition to the polysomnographic EEG montage, midline EEGs were recorded from 6 scalp electrode sites including Fz, FCz, Cz, CPz, Pz, and Oz. All EEG activities were referenced to linked mastoids. Four additional electrodes were placed above and below the left eye to record vertical eye movement and laterally to each eye to record horizontal EOG. A ground electrode was placed on the forehead. Electrode impedances were kept below 5 kΩ. The EEG and EOG were amplified by SYNAMPS amplifiers (Neuroscan, El Paso, TX) and sampled at 500 Hz with the digital band-pass filter set at 0.05–50 Hz.

Our previous studies (Hsieh et al., 2009; Tsai et al., 2005) showed that, while performing a flanker task, the EEG power density at certain frequency bands was changed after total sleep deprivation. Thus, we examined the extent to which SF affected EEG power. The EEG recorded at C3 underwent power spectral analysis using Fast Fourier transforms using the Hanning window. Each EEG data segment was 512 ms (256 samples), from 700 to 190 ms before the onset of the arrow array, and would be excluded from statistical analysis if it contained absolute EEG amplitudes higher than 50 μV or with a total power value outside a range limit which was determined individually and defined as the median plus/minus twice the interquartile range (the difference between the 25th and the 75th percentile) for each task test. Power density values were summed at 2.0–23.4 Hz (total), 2–3.9 Hz (delta), 5.9–7.8 Hz (theta), 9.8–11.7 Hz (alpha), 13.7–15.6 Hz (sigma), and 17.6–23.4 Hz (beta). The power density value at each frequency band for each artifact-free EEG segment was then logarithmically transformed.

For ERP analysis, the midline EEG data were high-pass filtered at 0.1 Hz (−12 dB) and were then segmented into stimulus-locked EEG epochs, 150 ms before to 800 ms

after the onset of the arrow stimuli, and into response-locked epochs, 200 ms before to 700 ms after key press. The stimulus-locked and response-locked EEG signals were baseline corrected between −100 and 0 ms and between −150 and −50 ms, respectively. The EEG epochs were then corrected by eye movement by using the Ocular Artifact Reduction command of SCAN v.4.3 (Neuroscan) and subsequently underwent movement artifact detection to exclude those containing absolute EEG amplitudes higher than 50 μV for waveform averaging. Differences in the mean number of EEG epochs included in stimulus-locked or response-clocked ERP analyses were not statistically significant between the LSF (454 ± 26 for congruent trial, 351 ± 49 for incongruent trial, 109 ± 49 for erroneous response, and 735 ± 90 for correct response) and HSF (437 ± 41 for congruent trial, 340 ± 72 for incongruent trial, 94 ± 39 for erroneous response and 697 ± 118 for correct response) conditions. The averaged ERPs were low-pass filtered at 10 Hz (−12 dB) before the 2nd-time baseline correction. In the stimulus-locked ERP, the N1 and N2 were defined as the most negative peak in windows from 140 to 260 ms and from 300 to 500 ms, respectively; the P300 was defined as the most positive peak in a window from 350 to 700 ms. In the response-locked ERP, the ERN and Pe were defined as the most negative peak value in a time window from 0 to 150 ms and the mean amplitude in a time window from 200 to 400 ms (Nieuwenhuis et al., 2001), respectively.

### 2.8. Salivary cortisol assay

Saliva samples collected in Salivette Cortisol were immediately centrifuged at 1000 × *g* for 10 min at 4 °C and frozen at −70 °C. Saliva samples were then sent to a local clinical diagnostic laboratory (Accuspeedy Medica Lab, Tainan, Taiwan), and the salivary cortisol was analyzed by an immunochemistry analyzer (Modular Analytics E170, Roche Diagnostics).

### 2.9. Statistical analysis

Differences between the 2 experimental conditions (HSF and LSF) were examined using paired *t* tests. Interaction effects between the 2 experimental conditions and the 2 study nights (adaptation and SF) or between the experimental conditions and the trial congruency (congruent vs. incongruent) conditions in the flanker task were evaluated using 2 × 2 repeated measures analyses of variances. Post hoc comparisons were performed using Tukey's honestly significant difference test. Pearson's coefficient of correlation ($r$) was calculated to evaluate the relation between the SF effect on sleep variables and the SF effect on ERP components and post-error compensations. The magnitude of SF effect on a certain variable was quantified by calculating the difference in variable values between the two SF conditions, e.g., the magnitude of SF effect on total sleep time (TST) = TST in HSF–TST in LSF. For subjective evaluations on sleep quality and sleepiness, Spearman's rank coefficient of correlation ($r_s$) was calculated to examine the relationship between the SF effect on subjective sleep variables and the SF effect on other measures. All statistical analyses were performed using SYSTAT 7.0 for Windows (Systat Software, Chicago, IL). The family-wise significance level was set at 0.05. Data are presented as mean ± SD.

## 3. Results

The sleep log data collected from the 13 participants (6 men and 7 women; 20–23 years old) showed that all maintained comparable sleep schedules (mean bedtime: 23:42 ± 00:08 vs. 23:42 ± 00:11; mean time of rising: 7:43 ± 00:17 vs. 7:42 ± 00:09) one week before the laboratory sleep study in the 2 experimental periods (LSF vs. HSF). The values of bedtime, time of rising, and time in bed derived from the actigraph data confirmed the sleep log data.

### 3.1. SF, sleep, and stress measures

On the LSF night, a mean of 558 ± 342 tone with a mean volume of 39.3 ± 2.0 dB and a mean duration of 9.9 ± 0.1 s were given and the mean number and percent of arousals associated with auditory stimuli were 13.2 ± 11.8 and 23.2 ± 16.1%, respectively. In contrast, the HSF night was associated with a lower mean number of auditory stimuli (305 ± 56; $t(12) = 2.55$, $p = 0.026$) but with a louder mean volume (92.7 ± 11.4 dB; $t(12) = 17.63$, $p < 0.001$) and a longer mean duration (32.0 ± 16.7 s; $t(12) = 4.77$, $p < 0.001$) and the mean number (90.1 ± 26.6; $t(12) = 10.20$, $p < 0.001$) and percent (66.2 ± 10.6%; $t(12) = 10.20$, $p < 0.001$) of arousals related to auditory stimuli were greater.

Compared to adaptation nights, the LSF treatment failed to induce significant changes in sleep architectures except for a slight increase in time in bed and thus in total sleep time (Table 1). Although the HSF treatment maintained a total sleep time comparable to that of the LSF night, it induced significant changes in several sleep parameters including increases in the amount of NREMS stage N1, decreases in the amount of both slow wave sleep (stage N3 sleep) and REMS. Furthermore, the HSF treatment doubled the number of sleep stage changes and arousals. The participants reported the worst sleep quality in the morning following the HSF night. The sleep variables that significantly varied with the experimental conditions on the SF nights as shown in Table 1 were further evaluated for the relation between the SF effect on sleep variables and the SF effect on subjective sleep quality evaluations. The percentage of slow wave sleep was the only sleep variable that showed a difference between

**Table 1**
Sleep variables obtained from laboratory sleep studies in the two experimental conditions.

| Variable | LSF | | HSF | | Significant effect |
|---|---|---|---|---|---|
| | Adaptation | SF | Adaptation | SF | |
| TIB (min) | 481 (4) | 487 (8)[a] | 481 (7) | 496 (4)[a,b] | E* N** E × N** |
| SOL (min) | 4.0 (2.9) | 4.1 (3.9) | 3.3 (2.7) | 2.8 (1.8) | |
| TST (min) | 466 (12) | 475 (12)[a] | 461 (23) | 477 (19)[a] | N** |
| TST-N1 (min) | 432 (18) | 441 (21) | 429 (29) | 383 (47)[a,b] | E** N* E × N** |
| NREMS (min) | 345 (21) | 349 (17) | 339 (21) | 378 (26)[a,b] | E* N** E × N** |
| REMS (min) | 121 (21) | 126 (16) | 122 (17) | 99 (26)[a,b] | E* E × N** |
| WASO (min) | 11.5 (9.4) | 7.5 (8.5) | 16.5 (20.7) | 16.8 (15.9) | |
| SE (%) | 96.7 (2.3) | 97.6 (2.2) | 95.8 (4.4) | 96.0 (3.3) | |
| Stage N1 (%) | 7.3 (2.4) | 7.2 (2.5) | 7.0 (3.1) | 19.8 (8.3)[a,b] | E** N** E × N** |
| Stage N2 (%) | 51.1 (4.1) | 52.3 (6.1) | 52.8 (5.0) | 55.2 (7.2) | |
| Stage N3 (%) | 15.6 (5.3) | 14.0 (5.2) | 13.8 (6.5) | 4.3 (4.1)[a,b] | E** N** E × N** |
| REMS (%) | 26.0 (4.2) | 26.5 (3.3) | 26.4 (3.3) | 20.7 (5.2)[a,b] | E* N* E × N** |
| SSC (no) | 126 (22) | 126 (16) | 129 (22) | 251 (50)[a,b] | E** N** E × N** |
| ArI (no/h) | 6.0 (1.9) | 6.1 (2.0) | 6.3 (2.4) | 15.7 (4.3)[a,b] | E** N** E × N** |
| SQ | 7.4 (1.7) | 7.5 (1.5) | 7.0 (1.3) | 4.7 (1.7)[a,b] | E** N** E × N** |

Data are presented as mean (SD). LSF, low-intensity sleep fragmentation; HSF, high-intensity sleep fragmentation; TIB, time in bed; SOL, sleep onset latency; TST, total sleep time; NREMS, non-rapid eye movement sleep; REMS, rapid-eye movement sleep; WASO, wakefulness after sleep onset; SE, sleep efficiency; Stage N1, NREMS stage N1; Stage N2, NREMS stage N2; N3, slow wave sleep; SSC, sleep stage changes; ArI, arousal index defined as the number of arousals per hour slept; SQ, sleep quality evaluated from 1 = extremely poor to 10 = extremely good; E, experimental condition effect (LSF vs. HSF); N, night effect (adaptation night vs. SF night).

* $p < 0.05$.

** $p < 0.01$ main and interactive effects of 2-factor (E × N) analysis of variances.

[a] $p < 0.05$ post hoc comparisons with the 2 adaptation nights using the Tukey test.

[b] $p < 0.05$ post hoc comparisons with the SF night in the LSF condition using the Tukey test.

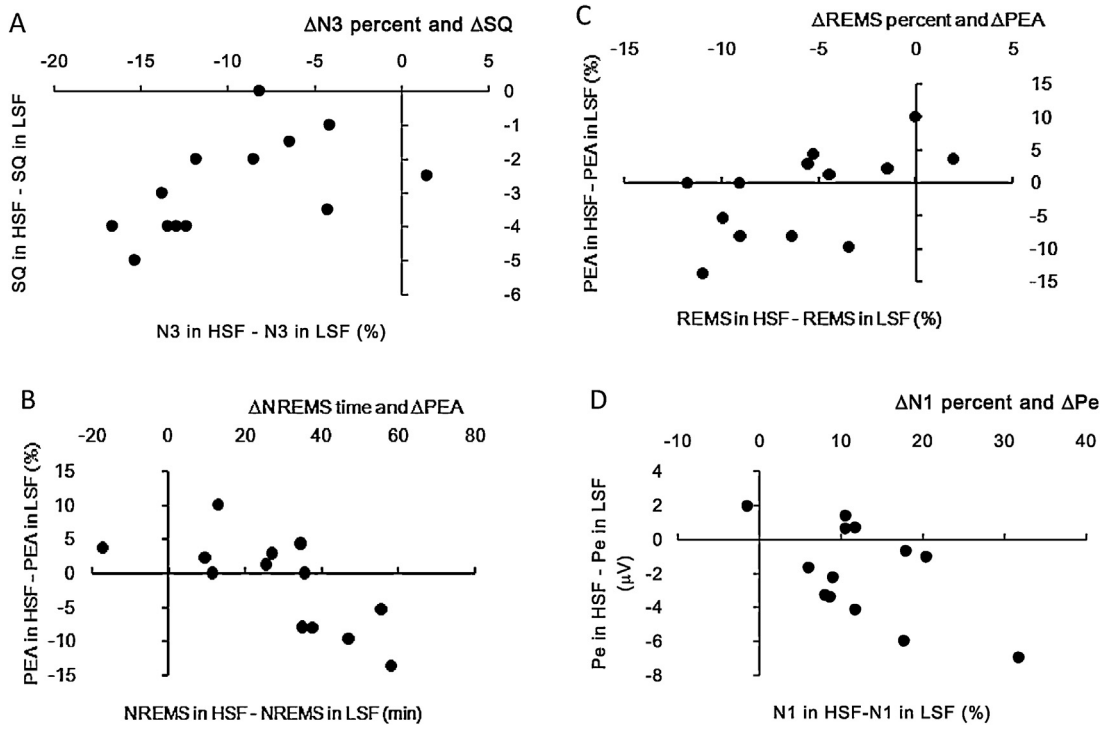


**Fig. 1.** Correlation analysis between sleep fragmentation condition differences in sleep variables and sleep fragmentation condition differences in (A) subjective evaluations on sleep quality (SQ), (B, C) post-error accuracy compensation (PEA), and (D) Pe amplitude. N3 refers to stage N3 sleep; NREMS, non-rapid eye movement sleep; REMS, rapid-eye movement sleep; N1, stage N1 sleep; LSF, low-level sleep fragmentation; HSF, high-level sleep fragmentation.

the two SF conditions significantly correlated with the difference in sleep quality values ($r_s = 0.700$, $p < 0.02$); as slow wave sleep was reduced by SF, sleep quality was worsened by SF (Fig. 1A).

Experimental condition effects were statistically significant on subjective stress evaluations upon morning awakenings and on heart rate variations during night sleep as shown in Table 2. However, the mean salivary cortisol level did not vary with experimental conditions or nights.

### 3.2. CPT and PASAT performance

Neither the interaction effect between the experimental condition and the previous night condition nor the main effect of the experimental condition on both the CPT and PASAT performance reached statistical significance (Table 3). The mean RT in the CPT was reduced following the 2nd night sleep (experimental nights) compared to the previous 1st night sleep (adaptation nights).

### 3.3. Flanker task

#### 3.3.1. Subjective evaluation and global behavioral performance

Participants felt sleepier, as represented by higher SSS scores, both before and after the flanker task on the day following the HSF night than the day following the LSF night (Table 4). However, the SF effect on SSS scores were not correlated with the SF effects on any sleep variables. Subjective evaluations on flanker task performance remained comparable between the LSF and HSF conditions.

The mean RT ($472 \pm 72$ ms in HSF vs. $447 \pm 43$ ms in LSF; $p = 0.089$) and the RT variability ($0.17 \pm 0.05$ in HSF vs. $0.15 \pm 0.03$ in LSF; $p = 0.09$) of correct responses in the flanker task tended to be greater following the HSF night but did not reach statistical significance. Response accuracy did not vary between the two SF conditions. Nonetheless, the congruency effect of test trials was statistically significant for response accuracy, mean RT and RT variability. Lower response accuracy rate, longer mean RT and greater RT variability were found more often in the incongruent trials than in the congruent trials.

**Table 2**
Stress measures.

| Variable | LSF | | HSF | |
|---|---|---|---|---|
| | Adaptation | SF | Adaptation | SF |
| Subjective evaluation | | | | |
| Bedtime | 1.6 (0.8) | 1.6 (0.8) | 2.5 (1.3) | 1.9 (1.2) |
| Morning awakening [E*] | 1.3 (0.5) | 1.3 (0.5) | 2.2 (1.4) | 1.6 (0.7) |
| Salivary cortisol (μg/dL) | 0.18 (0.07) | 0.18 (0.06) | 0.18 (0.07) | 0.20 (0.09) |
| Heart rate in sleep (bpm) | | | | |
| Average | 60.9 (5.0) | 59.5 (4.7) | 61.1 (6.1) | 61.1 (7.2) |
| Standard deviation [E**] | 5.4 (0.9) | 5.3 (0.7) | 5.6 (0.9) | 5.9 (0.9) |

Data are presented as mean (SD). LSF, low-intensity sleep fragmentation; HSF, high-intensity sleep fragmentation; bpm, beat per minute; E, experimental condition effect; N, night effect. Subjective stress levels were evaluated from 1 = extremely low to 10 = extremely high.

* $p < 0.05$.

** $p < 0.01$ experimental condition effects of 2-factor (E × N) analysis of variances.

**Table 3**
Continuous Performance Test (CPT) and Paced Auditory Serial Addition Task (PASAT) performed in the morning following each laboratory sleep night.

| Variable | LSF | | HSF | |
|---|---|---|---|---|
| | Adaptation | SF | Adaptation | SF |
| CPT | | | | |
| Correct RT (ms) [N*] | 449 (50) | 443 (45) | 454 (50) | 442 (60) |
| Omission error rate (%) | 0.2 (0.3) | 0.4 (1.5) | 0.2 (0.5) | 0.2 (0.3) |
| Commission error rate (%) | 11.5 (8.8) | 11.8 (12.5) | 10.3 (5.9) | 13.4 (9.0) |
| PASAT | | | | |
| Correct for 4-s interval (no) | 45.5 (4.9) | 46.8 (3.1) | 44.5 (7.5) | 46.0 (4.3) |
| Correct for 2-s interval (no) | 39.2 (9.9) | 40.4 (11.5) | 38.4 (11.9) | 41.3 (9.6) |

Data are presented as mean (SD). LSF, low-intensity sleep fragmentation; HSF, high-intensity sleep fragmentation; RT, reaction time; E, experimental condition effect; N, night effect.
* $p < 0.05$ night effects of 2-factor (E × N) analysis of variances.

### 3.3.2. Post-error behavioral performance

As sleep disruptions might reduce the capability of post-error behavioral compensatory effects, we first examined which response variable(s) of accuracy, error rate, omission rate, and mean RT of correct responses maintained statistically significant differences between post-error trials and post-correct trials in the LSF condition. Significant post-error compensatory effects were found in response accuracy ($t(12) = 3.93$, $p = 0.002$) and error rate ($t(12) = 4.26$, $p = 0.001$) but not in omission rate ($p = 0.787$) or in mean RT in the case of the correct trials ($p = 0.247$). The response accuracy ($88.7 \pm 5.0\%$ in post-error trials vs. $84.9 \pm 5.8\%$ in post-correct trials) increased in the trials following erroneous responses. Post-error compensatory effects on response accuracy in the HSF condition were subsequently evaluated; however, they failed to show statistical significance ($86.9 \pm 8.7\%$ in post-error trials vs. $84.5 \pm 7.7\%$ in post-correct trials; $p = 0.253$). A 3-factor analysis of variances was further performed but failed to show a significant interaction effect between SF conditions and post-error improvements on response accuracy ($p = 0.436$).

As comparisons of mean correct RTs calculated from all post-error trials failed to show significant post-error compensatory effects on RT, we also applied the method suggested by Dutilh et al. (2012) to examine the compensatory effect on RT and to eliminate the possible confounds of global fluctuations in performance over the course of the task. When mean correct RTs derived from post-correct trials that are also pre-error trials were compared with mean correct RTs in post-error trials, a post-error slowing effect was found in both the LSF ($445 \pm 44$ ms in post-error trials vs. $428 \pm 48$ ms in post-correct trials, $t(12) = 3.46$, $p = 0.005$) and HSF ($479 \pm 80$ ms in post-error trials vs. $449 \pm 71$ ms in post-correct trials, $t(12) = 5.49$, $p < 0.001$) conditions. However, the magnitude of post-error slowing was not significantly different between the two SF conditions ($p = 0.258$).

Since the post-error compensatory effect on response accuracy was significant in the LSF condition but not in the HSF condition, we explored whether differences in post-error accuracy compensations between the two SF conditions were related to differences in sleep variables. The PSG sleep variables with an SF effect correlated significantly with the post-error accuracy compensation including NREMS time ($r = -0.710$, $p = 0.007$) and the percentage of REMS ($r = 0.579$, $p = 0.038$); as NREMS time increased and REMS percent decreased, the post-error accuracy compensation was reduced in the HSF condition (Fig. 1B and C).

### 3.3.3. Electrophysiological data

EEG power density at none of the frequency bands differed between the two SF conditions. As shown in Table 5 and Fig. 2, the latency and amplitude of the stimulus-locked ERP components N1 at Oz and N2 at FCz did not differ between the two SF conditions. Although the latency of P300 at Pz did not vary with the SF condition, the peak amplitude of P300 was reduced in the HSF condition (SF main effect: $F(1,12) = 5.47$, $p = 0.038$). The peak latency and amplitude of the response-locked ERP component ERN at FCz maintained comparable values between the two SF conditions (Table 5 and Fig. 3). However, the mean amplitude of Pe at Cz was reduced in the HSF condition ($t(12) = 2.48$, $p = 0.029$).

None of the sleep variables with an SF effect correlated significantly with the SF effect on the P300 amplitudes. The percentage of

**Table 4**
Flanker task performance and subjective evaluation in the morning following each sleep fragmented (SF) night.

| Variable | LSF | | HSF | |
|---|---|---|---|---|
| | Congruent | Incongruent | Congruent | Incongruent |
| Correct RT, ms [E+C**] | 416 (43) | 489 (42) | 441 (73) | 515 (74) |
| Correct RTV [E+C**] | 0.14 (0.04) | 0.11 (0.03) | 0.16 (0.06) | 0.14 (0.06) |
| Accuracy (%) [C**] | 97.0 (3.8) | 74.1 (8.6) | 97.2 (3.0) | 72.9 (13.6) |
| Error rate (%) [C**] | 2.5 (3.5) | 25.1 (8.2) | 2.5 (2.9) | 26.2 (13.7) |
| Omission rate (%) [C+] | 0.5 (0.9) | 0.8 (1.0) | 0.3 (0.7) | 0.9 (1.3) |
| SSS [E#] | | | | |
| Before task test | 2.8 (1.1) | | 3.3 (1.2) | |
| After task test | 2.8 (1.2) | | 3.3 (1.5) | |
| Estimated accuracy (%) | 70.4 (11.3) | | 72.9 (9.8) | |
| Certainty of accuracy estimation | 7.3 (1.3) | | 7.0 (1.5) | |
| Effort for task performance | 8.5 (1.0) | | 8.6 (1.1) | |

Data are presented as mean (SD). LSF, low-intensity sleep fragmentation; HSF, high-intensity sleep fragmentation; RT, reaction time; RTV, intra-individual reaction time variability defined as the standard deviation of RT in a test divided by the mean RT in that test; SSS, Stanford Sleepiness Scale; E, experimental condition effect; C, trial congruency effect.
+ $p < 0.1$.
* $p < 0.05$.
** $p < 0.01$ main effects of 2-factor (E × C) analysis of variances.
# $p < 0.05$ main experimental condition effects of 2-factor (before vs. after test × LSF vs. HSF night) analysis of variances.

**Table 5**
Stimulus-locked and response-locked event-related potential (ERP) components during the Flanker task test.

| Variable | LSF | | HSF | |
|---|---|---|---|---|
| | Congruent | Incongruent | Congruent | Incongruent |
| Stimulus-locked ERP | | | | |
| Peak latency | | | | |
| N1 at Oz | 208 (31) | 213 (25) | 214 (24) | 213 (24) |
| N2 at FCz | NA | 428 (30) | NA | 433 (37) |
| P300 at Pz | 484 (72) | 550 (39) | 487 (80) | 546 (51) |
| Peak amplitude | | | | |
| N1 at Oz | −4.1 (3.0) | −4.1 (3.0) | −4.1 (2.9) | −4.2 (3.0) |
| N2 at FCz | NA | 1.4 (3.9) | NA | 1.7 (3.4) |
| P300 at Pz [E* C**] | 14.6 (4.2) | 16.2 (5.0) | 13.7 (4.0) | 15.2 (4.8) |
| Response-locked ERP | | | | |
| Peak latency | | | | |
| ERN at FCz | 51 (12) | | 44 (22) | |
| Amplitude | | | | |
| ERNp at FCz | −4.7 (2.4) | | −3.8 (2.8) | |
| Pe at Cz | 11.2 (5.2) | | 9.3 (5.3)# | |

Data are presented as mean (SD). LSF, low-intensity sleep fragmentation; HSF, high-intensity sleep fragmentation; NA, not available; E, experimental condition effect; C, trial congruency effect; ERNp, peak amplitude for ERN. Mean amplitude is presented for Pe.

* $p < 0.05$.

** $p < 0.01$ main effects of 2-factor (E × C) analysis of variances.

\# $p < 0.05$ comparisons between the two SF nights by using paired-$t$ tests.

NREMS stage N1 was the only sleep variable showing an SF effect that correlated significantly with the Pe amplitude ($r = -0.590$, $p = 0.034$); as N1 sleep time was increased by SF, the Pe amplitude was greatly reduced in the HSF condition (Fig. 1D).

## 4. Discussion

Compared to the LSF condition, which served as a control condition for frequent but mild sleep disturbing auditory stimulation during sleep, the HSF protocol with the extended time in bed maintained a comparable total sleep time but successfully doubled the arousals and sleep stage changes. Similar to previous studies (Cote et al., 2003; Kingshott et al., 2000; Martin et al., 1996; Philip et al., 1994), the HSF inevitably led to changes in sleep stage distribution, including increases in stage N1 sleep and decreases in both slow wave sleep and REMS (see Table 1). However, these sleep stage changes at the HSF night did not result in increases in EEG power density over the course of task performance on the following day, as was the case after 1 night of total sleep deprivation (Tsai et al., 2005). Furthermore, in contrast to an elevation in morning cortisol level induced by 2 nights of SF achieved by using both auditory and mechanical stimuli (Stamatakis & Punjabi, 2010), the cortisol level in the morning following 1 night of SF did not significantly differ from that in the morning following adaptation nights or between the HSF and LSF conditions. Taken together, the SF protocols used in this study appear to induce mild, if any, total sleep loss and hormonal stress responses. Differences in behavioral and electrophysiological outcomes between the two SF treatments may thus be related to changes in sleep architecture or increases in sleep disruptions caused by HSF.

Following 1 night of HSF, subjective evaluations on sleep quality decreased and subjective sleepiness increased. Although behavioral performances on CPT, PASAP, and flanker tasks requiring sustained attention, information processing, and higher executive control remained comparable between the two SF conditions, two electrophysiological measures showed significant SF effects. Both the P300 amplitude, which reflects attentional processes (Picton, 1992; Polich, 2007), and the Pe amplitude, which is an electrophysiological index of error monitoring functions and hypothesized to reflect error awareness (Murphy et al., 2012; Nieuwenhuis et al., 2001) and emotional evaluation of errors (Hajcak et al., 2003), were reduced in the HSF condition.

Our data confirm the previous findings that SF with unchanged total sleep time may still cause increased subjective (Cote et al., 2003; Kingshott et al., 2000) and objective, e.g., multiple sleep latency test (Martin et al., 1996; Philip et al., 1994; Roehrs et al., 1994; Stepanski et al., 1987), daytime sleepiness but not jeopardize most cognitive performance (Cote et al., 2003; Kingshott et al., 2000; Philip et al., 1994). The idea that neurophysiologic measures are more sensitive than behavioral measures for revealing impairment associated with increased daytime sleepiness resulting from SF (Cote et al., 2003; Kingshott et al., 2000) was also supported by the findings of P300 amplitudes decreased by HSF. Our data further provide 2 new findings on the effect of SF.

First, participants did indicate poorer sleep quality on their HSF night sleep even though the total sleep time was not reduced. The SF effect on sleep quality was related to the magnitude of reduction in slow wave sleep time. EEG slow wave activity is a major marker of NREMS homeostasis (Borbély & Achermann, 1999). The slow wave sleep time may somewhat reflect sleep intensity since slow wave sleep contains more slow wave activity than other sleep stages as its name indicates. Reductions in slow wave sleep time caused by SF may represent reductions in sleep intensity and thus led to subjective evaluations of poorer sleep quality. On the other hand, poorer sleep quality in the HSF condition was unlikely to be correlated with a higher stress level, reflected by subjective stress evaluations and heart rate variations (see Table 2), since poor sleep quality was presented only following the HSF night and stress-related changes were found following both the previous adaptation night and the HSF night.

Second, in addition to the P300 amplitude, a neurophysiologic measure on attention processing, the Pe amplitude, a neurophysiologic measure on error monitoring, was altered by SF. Furthermore, changes in the Pe amplitude negatively related to changes in the N1 sleep time. Since the ERN amplitude was not changed in the HSF condition, the notion that the Pe appears more sensitive to sleepiness resulting from mild sleep loss or sleep disruption than the ERN as proposed in the Introduction was further supported. Thus, sleepiness, enhanced by SF, might not be adequate to alter the processing of error detection (reflected by the ERN amplitude) but rather functions to sufficiently impair the ability to be aware of errors or to evaluate the significance of errors (reflected by the Pe amplitude). On the other hand, whether increases in light N1 sleep or reductions in deep non-N1 sleep mediated the impairment

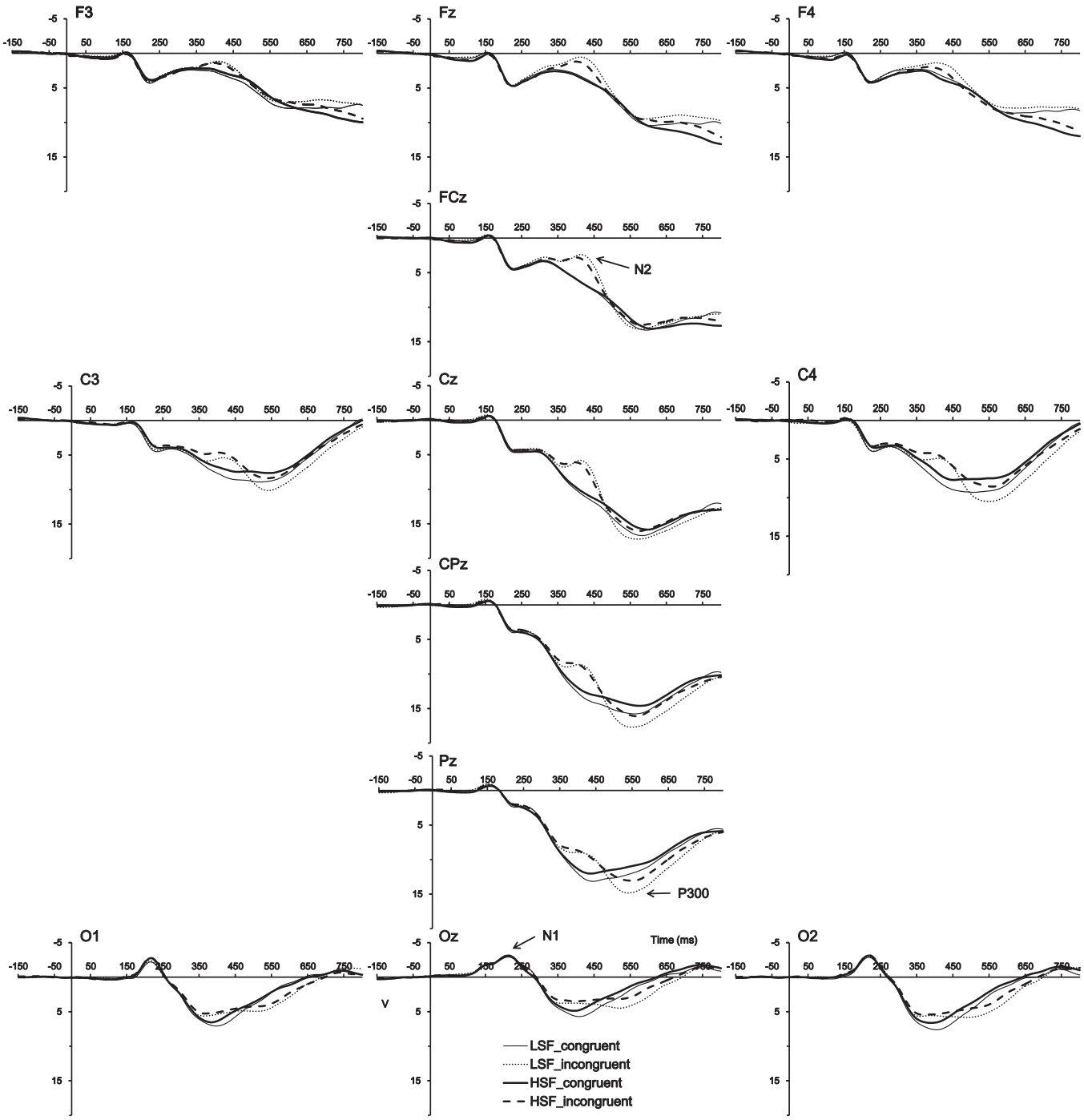


**Fig. 2.** Grand average stimulus-locked event-related potential waveforms for congruent and incongruent trials with correct responses, respectively. The onset of array stimuli is at 0 ms. LSF refers to low-level sleep fragmentation; HSF, high-level sleep fragmentation.

in the Pe amplitude needs to be examined in the future study. In contrast to electrophysiological findings on error monitoring, behavioral deficits in post-error slowing and post-error accuracy compensation did not reach statistical significance, although the magnitude of post-error accuracy compensation appeared reduced in the HSF condition. Thus, the findings on error monitoring also suggest that neurophysiologic measures are more sensitive than behavioral measures for revealing impairment caused by mild sleep disruptions. However, given that the magnitudes of changes in the NREMS and REMS time between the two SF conditions were oppositely correlated with changes in post-error accuracy compensation but not correlated with changes in the Pe amplitude, changes in specific sleep stages might affect specific error monitoring functions.

Although SF resulted in reductions in both the P300 and the Pe amplitudes, the SF effect on P300 amplitudes were not significantly correlated with the SF effect on the Pe amplitude. Furthermore, the SF effect on N1 sleep time was correlated with the SF effect on the Pe amplitude but not related to the SF effect on P300 amplitudes. Thus, even though the P300 and Pe are intimately related to each other (Davies et al., 2001) and might reflect similar neurocognitive processes involved in the conscious processing of motivationally

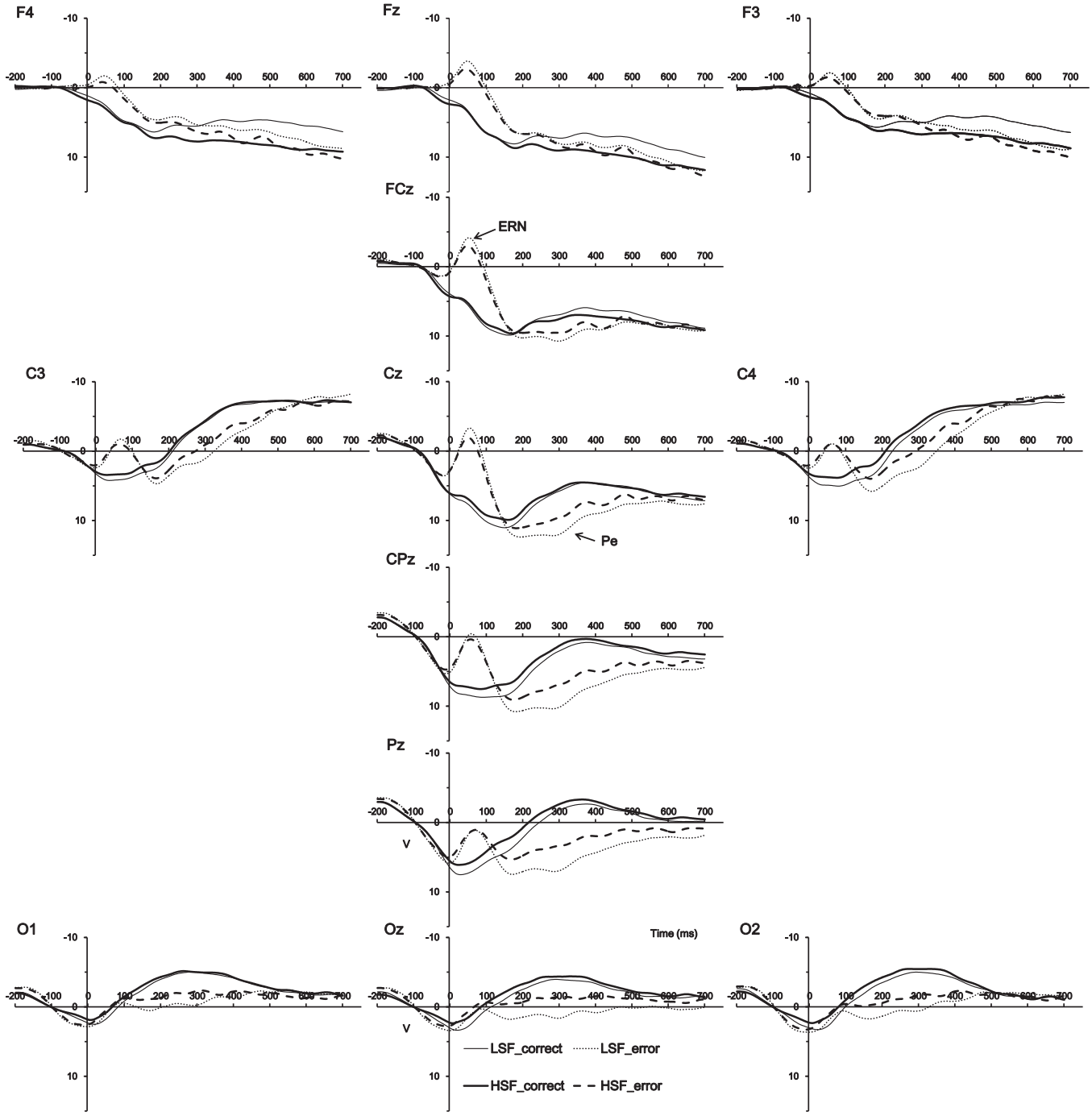


**Fig. 3.** Grand average response-locked event-related potential waveforms for trials with correct and erroneous responses, respectively. Response onset occurs at 0 ms. LSF refers to low-level sleep fragmentation; HSF, high-level sleep fragmentation; ERN, error-related negativity; Pe, error positivity.

significant events (Ridderinkhof et al., 2009), they may respond to increased sleepiness induced by frequent disruptions in sleep continuity via different mechanisms.

In summary, this study applied frequent auditory stimulation to night sleep and found that high-level sleep disruptions, relative to low-level sleep disruptions, resulted in poorer sleep quality, increased subjective daytime sleepiness, and decreased attention and error monitoring processing. Theses SF effects appeared to involve different sleep mechanisms, including the correlation between changes in sleep quality and changes in deep NREMS stage time, between changes in NREMS/REMS time and changes in post-error accuracy compensations, and between changes in light sleep time and changes in Pe amplitudes. Although one night of SF resulted in subtle impairment in error monitoring, whether the error monitoring function would continue to deteriorate, habituate, or compensate in chronic SF requires further study.

## Conflicts of interest

This was not an industry supported study. All authors report no financial conflicts of interest.

## Acknowledgements

We sincerely thank Yu-Chi Liang and Yun-Hsuan Chen for their assistantship with all the experiments. The authors gratefully acknowledge the financial support from National Science Council, Taiwan, ROC (Grant No. NSC99-2314-B-194-001-MY2).

## References

Asaoka, S., Fukuda, K., Murphy, T. I., Abe, T., & Inoue, Y. (2012). The effects of a nighttime nap on the error-monitoring functions during extended wakefulness. *Sleep*, *35*(6), 871–878.

Beck, A. T., Epstein, N., Brown, G., & Steer, R. A. (1988). An inventory for measuring clinical anxiety: Psychometric properties. *Journal of Consulting and Clinical Psychology*, *56*, 893–897.

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Manual for the Beck Depression Inventory-II*. San Antonio, Texas: Psychological Corporation.

Bonnet, M. H., & Arand, D. L. (2003). Clinical effects of sleep fragmentation versus sleep deprivation. *Sleep Medicine Review*, *7*(4), 297–310.

Borbély, A. A., & Achermann, P. (1999). Sleep homeostasis and models of sleep regulation? *Journal of Biological Rhythms*, *14*(6), 557–568.

Cote, K. A., Milner, C. E., Osip, S. L., Ray, L. B., & Baxter, K. D. (2003). Waking quantitative electroencephalogram and auditory event-related potentials following experimentally induced sleep fragmentation. *Sleep*, *26*, 687–694.

Davies, P. L., Segalowitz, S. J., Dywan, J., & Pailing, P. E. (2001). Error negativity and positivity as they relate to other ERP indices of attentional control and stimulus processing. *Biological Psychology*, *56*, 191–206.

Dutilh, G., van Ravenzwaaij, D., Nieuwenhuis, S., van der Maas, H. L., Forstmann, B. U., & Wagenmakers, E. J. (2012). How to measure post-error slowing: A confound and a simple solution. *Journal of Mathematical Psychology*, *56*, 208–216.

Eriksen, B. A., & Eriksen, C. W. (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task. *Perception & Psychophysics*, *16*, 143–149.

Fiehler, K., Ullsperger, M., & von Cramon, D. Y. (2004). Neural correlates of error detection and error correction: Is there a common neuroanatomical substrate? *European Journal of Neuroscience*, *19*, 3081–3087.

Gehring, W. J., Goss, B., Coles, M. G. H., Meyer, D. E., & Donchin, E. (1993). A neural system for error detection and compensation. *Psychological Science*, *4*, 385–390.

Gronwall, D. M. (1977). Paced auditory serial-addition task: A measure of recovery from concussion. *Perceptual and Motor Skills*, *44*, 367–373.

Hajcak, G., McDonald, N., & Simons, R. F. (2003). To err is autonomic: Error-related brain potentials, ANS activity, and post-error compensatory behavior. *Psychophysiology*, *40*, 895–903.

Hoddes, E., Zarcone, V., Smythe, H., Phillips, R., & Dement, W. C. (1973). Quantification of sleepiness: A new approach. *Psychophysiology*, *10*, 431–436.

Horne, J. A., & Ostberg, O. (1976). A self-assessment questionnaire to determine morningness–eveningness in human circadian rhythms. *International Journal of Chronobiology*, *4*, 97–110.

Hsieh, S., Cheng, I.-C., & Tsai, L.-L. (2007). Immediate error correction process following sleep deprivation. *Journal of Sleep Research*, *16*, 137–147.

Hsieh, S., Li, T.-H., & Tsai, L.-L. (2010). Impact of monetary incentives on cognitive performance and error monitoring following sleep deprivation. *Sleep*, *33*, 499–507.

Hsieh, S., Tsai, C.-Y., & Tsai, L.-L. (2009). Error correction maintains posterior adjustments after one night of total sleep deprivation. *Journal of Sleep Research*, *18*, 159–166.

Iber, C., Ancoli-Israel, S., Chesson, A. L., Jr., & Quan, S. F. (2007). *The AASM manual for the scoring of sleep and associated events: Rules, terminology and technical specifications*. Westchester, IL: American Academy of Sleep Medicine.

Johns, M. W. (1991). A new method for measuring daytime sleepiness: The Epworth Sleepiness Scale. *Sleep*, *14*, 540–545.

Kingshott, R. N., Cosway, R. J., Deary, I. J., & Douglas, N. J. (2000). The effect of sleep fragmentation on cognitive processing using computerized topographic brain mapping. *Journal of Sleep Research*, *9*, 353–357.

Laming, D. (1968). *Information theory of choice reaction times*. London: Academic Press.

Laming, D. (1979). Choice reaction performance following an error. *Acta Psychologica*, *43*, 199–224.

Martin, S. E., Engleman, H. M., Deary, I. J., & Douglas, N. J. (1996). The effect of sleep fragmentation on daytime function. *American Journal of Respiratory and Critical Care Medicine*, *153*, 1328–1332.

Martin, S. E., Wraith, P. K., Deary, I. J., & Douglas, N. J. (1997). The effect of nonvisible sleep fragmentation on daytime function. *American Journal of Respiratory and Critical Care Medicine*, *155*, 1596–1601.

Murphy, T. I., Richard, M., Masaki, H., & Segalowitz, S. J. (2006). The effect of sleepiness on performance monitoring: I know what I am doing, but do I care? *Journal of Sleep Research*, *15*, 15–21.

Murphy, P. R., Robertson, I. H., Allen, D., Hester, R., & O'Connell, R. G. (2012). An electrophysiological signal that precisely tracks the emergence of error awareness. *Frontiers in Human Neuroscience*, *6*, 65. http://dx.doi.org/10.3389/fnhum.2012.00065

Nieuwenhuis, S., Ridderinkhof, K. R., Blom, J., Band, G. P., & Kok, A. (2001). Error-related brain potentials are differentially related to awareness of response errors: Evidence from an antisaccade task. *Psychophysiology*, *38*, 752–760.

Philip, P., Stoohs, R., & Guilleminault, C. (1994). Sleep fragmentation in normals: A model for sleepiness associated with upper airway resistance syndrome. *Sleep*, *17*, 242–247.

Picton, T. W. (1992). The P300 wave of the human event-related potential. *Journal of Clinical Neurophysiology*, *9*, 456–479.

Polich, J. (2007). Updating P300: An integrative theory of P3a and P3b. *Clinical Neurophysiology*, *118*(10), 2128–2148.

Rabbitt, P. M. A. (1966). Errors and error correction in choice-response tasks. *Journal of Experimental Psychology*, *71*, 264–272.

Ramdani, C., Carbonnell, L., Rabat, A., Meckler, C., Burle, B., Hasbroucq, T., et al. (2013). Sleep deprivation affects the sensitivity of proactive and reactive action monitoring: A behavioural and ERP analysis. *Biological Psychology*, *93*, 237–245.

Renn, R. P., & Cote, K. A. (2013). Performance monitoring following total sleep deprivation: Effects of task type and error rate. *International Journal of Psychophysiology*, *88*, 64–73.

Reynolds, A. C., & Banks, S. (2010). Total sleep deprivation, chronic sleep restriction and sleep disruption. *Progress in Brain Research*, *185*, 91–103.

Ridderinkhof, K. R., Ramautar, J. R., & Wijnen, J. G. (2009). To $P_E$ or not to $P_E$: A P3-like ERP component reflecting the processing of response errors. *Psychophysiology*, *46*, 531–538.

Roehrs, T., Merlotti, L., Petrucelli, N., Stepanki, E., & Roth, T. (1994). Experimental sleep fragmentation. *Sleep*, *17*, 438–443.

Rosvold, H. E., Mirsky, A. F., Sarason, I., Bransome, E. D., Jr., & Beck, L. H. (1956). A continuous performance test of brain damage. *Journal of Consulting Psychology*, *20*, 343–350.

Sadeh, A., Gruber, R., & Raviv, A. (2002). Sleep, neurobehavioral functioning, and behavior problems in school-age children. *Child Development*, *73*, 405–417.

Scheffers, M. K., Humphrey, D. G., Stanny, R. R., Kramer, A. F., & Coles, M. G. (1999). Error-related processing during a period of extended wakefulness. *Psychophysiology*, *36*, 149–157.

Stamatakis, K. A., & Punjabi, N. M. (2010). Effects of sleep fragmentation on glucose metabolism in normal subjects. *Chest*, *137*, 95–101.

Stepanski, E. (2002). The effect of sleep fragmentation on daytime function. *Sleep*, *25*, 268–276.

Stepanski, E., Lamphere, J., Roehrs, T., Zorick, F., & Roth, T. (1987). Experimental sleep fragmentation in normal subjects. *International Journal of Neuroscience*, *33*, 207–214.

Tsai, L.-L., Young, H.-Y., Hsieh, S., & Lee, C.-S. (2005). Impairment of error monitoring following sleep deprivation. *Sleep*, *28*, 707–713.